FDA Plasma Standards Workshop

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Bayer Plasma Summary

Raw Material	pdFVIII	IGIV IGIM	Alpha$_1$-PI	Albumin PPF
Source Plasma	Yes	Yes	Yes *and* Fr IV-1 Paste Intermediate	Yes
Recovered Plasma	No	No	Fr IV-1 Paste Intermediate	No

Bayer Plasma Summary

Raw Material	Freeze Temp.	Store Temp.	Ship Temp.	Time to Expiry
Source Plasma (Plasmapheresis)	-20ºC or Colder	-20ºC or Colder	-20ºC or Colder	3 Years
Plasma Used to Produce Fr IV-1 Paste Intermediate	**SP** -20ºC or Colder **RP** -18ºC or Colder	**SP** -20ºC or Colder **RP** -18ºC or Colder	**SP** and **RP**: -20ºC or Colder	As Specified by Fractionator

Bayer Source Plasma Specifications

- Plasma is considered suitable for fractionation for the US market if the following conditions are fulfilled
  - The total period of time during which the temperature exceeds -20ºC does not exceed 72 hours and the plasma remains frozen solid during storage
  - The temperature at no time exceeds +10ºC
    - 21 CFR §640.76
- Plasma is considered suitable for fractionation for Europe if the following conditions are fulfilled
  - The total period of time during which the temperature exceeds -20ºC does not exceed 72 hours
  - The temperature does not exceed -15ºC on more than one occasion
  - The temperature at no time exceeds -5ºC
    - EP Monograph *Human Plasma for Fractionation*

On the Use of Plasma Derived from Whole Blood (Recovered Plasma)

- Bayer does not currently fractionate recovered plasma for commercial product manufacture and distribution
- Bayer manufactures Alpha$_1$-Proteinase Inhibitor from Fraction IV-1 paste intermediates
  - Recovered Plasma stored at -18°C or colder and shipped at -20°C or colder
  - Source Plasma stored and shipped at -20°C or colder
  - Fraction IV-1 paste stored and shipped at -20°C or colder
- Alpha$_1$-Proteinase Inhibitor manufactured from intermediate paste has the same final product specifications and shelf-life with no differences in the final product stability as compared to Alpha$_1$-Proteinase Inhibitor manufactured from Source Plasma

Bayer Supporting Data Summary

- Bayer Plasma Stability Study (10 year study)
  - Data available for 3 years of storage for Source Plasma collected by plasmapheresis
  - Stability indicating parameters monitored: FVIII potency, anti-HBs Ag potency
- Source Plasma collected from 52 random donors was thawed, pooled and transferred to polyethylene plasma collection bottles
- Polyethylene bottles stored at -20°C or colder and thawed at 5°C for 19 hours prior to testing
- Evaluation of the pooled data trend for the parameters monitored indicate:
  - FVIII potency - no significant change through 36 months
  - Anti-HBs Ag potency - no significant change through 36 months

Conclusions

- The existing US regulations regarding freezing, storage and transport of plasma for fractionation have been in place for decades and have served the consumers and industry well
- The decreased demand of pdFVIII brings into question the need to invest millions into increasing factor VIII yield through plasma collection activities
- In the absence of a demonstrated improvement in the quality of derivatives manufactured from plasma frozen rapidly after collection, manufacturers should be afforded the flexibility to improve yield through processing innovation and optimization